PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference S30F1809	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/JP2005/020302	International filing date *(day/month/year)* 04 November 2005 (04.11.2005)	Priority date *(day/month/year)* 05 November 2004 (05.11.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant SENJU PHARMACEUTICAL CO., LTD.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 08 May 2007 (08.05.2007)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Yoshiko Kuwahara e-mail: pt07.pct@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference S30F1809	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2005/020302	04.11.2005	05.11.2004

International Patent Classification (IPC) or both national classification and IPC

Applicant
SENJU PHARMACEUTICAL CO., LTD.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Date of completion of this opinion	Authorized officer
Facsimile No.		Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2005/020302

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ the translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rule 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing

      ☐ contained in the international application as filed

      ☐ filed together with the international application in electronic form

      ☐ furnished subsequently to this Authority for the purposes of search

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 1-12

because:

☒ the said international application, or the said claims Nos. 1-12 relate to the following subject matter which does not require an international search (*specify*):

The inventions of claims 1-12 relate to a method for treating the human or animal body by surgery or therapy, and therefore are not subject to review by this International Searching Authority in accordance with PCT Article 34(4)(a)(i) and PCT Rule 67.1(iv).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for said claims Nos. 1-12

☐ a meaningful opinion could not be formed without the sequence listing: the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings: the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	15-24, 27-35	YES
	Claims	12, 14, 25, 26	NO
Inventive step (IS)	Claims	16-24, 28-35	YES
	Claims	13-15, 25-27	NO
Industrial applicability (IA)	Claims	13-35	YES
	Claims		NO

2. Citations and explanations:

This opinion is presented based on the following documents listed in the International Search Report.

Document 1: JP 02-124817 A (SENJU PHARM CO) 14 May 1990
Document 2: JP 11-335301 A (NIPPON OILS & FATS CO., LTD.) 7 December 1999
Document 3: JP 08-291065 A (SANTEN PHARM CO., LTD.) 5 November 1996
Document 4: JP 2002-114711 A (LION CORP.) 16 April 2002
Document 5: WO 96/19211 A1 (TAISHO PHARM CO., LTD.) 27 June 1996

○ Claims 13, 14, 25, and 26

Document 1 describes an aqueous ophthalmologic agent in the form of eye drops for the treatment of inflammatory diseases of the external or anterior eye containing 2-amino-3-(4-bromobenzoyl) phenylacetic acid and sodium edetate, benzalkonium chloride, and EDTA. In addition, document 1 (page 2, lower right column, lines 2 to 17) states that in an ophthalmologic solution, retention of the active ingredient at the site of inflammation for a requisite period of time is important for the desired therapeutic effect of the drug to be expressed.

Document 1 does not describe maintaining a therapeutically effective concentration of 2-amino-3-(4-bromobenzoyl) phenylacetic acid in the aqueous humor over at least 24 hours by administration of eyedrops once a day, but because the aforementioned sodium edetate and the like are all organic amines, it is extremely likely that in the aqueous ophthalmologic agent in the form of eyedrops described in document 1, a therapeutically effective concentration will be maintained for at least 24 hours.

Therefore, the inventions of claims 13, 14, 25, and 26 do not appear to possess novelty and involve an inventive step with respect to document 1.

○ Claims 13-15 and 25-27

The inventions of the above claims differ from the invention described in document 1 with respect to the inclusion of an organic amine other than sodium edetate and the like.

However, document 2 (CLAIMS, Paragraph 0050) states that a drug ingredient such as an anti-inflammatory agent and the like can be retained for a long period of time and the expression of therapeutic efficacy of the drug ingredient can be enhanced by including the organic amine represented by General Formula (1) in an ophthalmologic agent.

(Continued in supplemental box)

WRITTEN OPINION OF THE
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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 13 and 14

An attempt has been made to specify the inventions of claims 13 and 14 by the results provided thereby, but in the DESCRIPTION only inventions that also contain an organic amine such as trometamol and the like in the specified amount are disclosed as EXAMPLES, and no clue is provided for obtaining these results in inventions other than ones containing an organic amine. As a result, claims 13 and 14 lack full disclosure in the sense of PCT Article 5 and lack support by the disclosure of the DESCRIPTION in the sense of PCT Article 6. Furthermore, when we take into consideration the level of technical knowledge available at the time this application was filed, claims 13 and 14 do not satisfy the requirement for clarity in the sense of PCT Article 6.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V.2

This being the case, this authority finds that it is obvious to persons skilled in the art to include the organic amine described in document 2 in the aqueous ophthalmologic agent in the form of eyedrops described in document 1 for long-term retention of therapeutic efficacy of the active ingredient.

Therefore, the inventions of claims 13-15 and 25-27 do not appear to involve an inventive step with respect to documents 1 and 2.

○ Claims 16-24 and 28-35

Document 3 (CLAIMS and Paragraph 0006) describe preparing an eyedrop solution having excellent stability and causing little irritation to the eye by including an organic amine such as tromethamine and the like in an ophthalmologic agent containing pranoprofen.

Document 4 (CLAIMS and Paragraph 0041) describe preparing an ophthalmologic composition with excellent stability of the therapeutic agent and enhanced efficacy thereof by including a polyvinyl alcohol and trometamol in an ophthalmologic composition containing a therapeutic agent.

Document 5 (CLAIMS and page 2, lines 8 to 9) states that a liposome ophthalmologic agent containing taurine, i.e. aminoethanesulfonic acid, glucose, and an inorganic salt has a long retention time on the surface of the cornea.

However, documents 1-5 neither disclose nor suggest the fact that a therapeutically effective concentration of 2-amino-3-(4-bromobenzoyl) phenylacetic acid can be maintained for a least 24 hours in the aqueous humor through administration of eyedrops once a day by containing therein the organic amine specified in the above claims at an octanol/water partition coefficient of 0.7 to 4.0.

This being the case, the inventions of claims 16-24 and 28-35 appear to be novel and involve an inventive step with respect to documents 1-5.